REMARKS

Any fees that may be due in connection with filing this paper or with this application may be charged to Deposit Account No. 50-1213. If a Petition for Extension of time is needed, this paper is to be considered such Petition.

A supplemental Information Disclosure Statement accompanies this response.

A sheet showing marked-up amended claim 1 pursuant to 37 C.F.R. §1.121 is attached hereto.

TRAVERSAL OF RESTRICTION REQUIREMENT

Claims 1-37 are presently pending and are subject to a Restriction Requirement and an Election of Species requirement. The Office Action sets forth forty (40) groups for election, and further sets forth a Requirement for Election of Species for each of the forty groups. Applicant respectfully traverses the restriction requirement.

It is respectfully submitted that the Restriction Requirement is improper. In order for restriction to be proper, under 37 C.F.R. §§1.141 and 1.142, the restricted subject matter must be independent or distinct **AND** there must be a burden on the Office to examine the claims in the claims in the same application. It is respectfully submitted that in this instance, the Office has failed to demonstrate either of these requirements.

Subject Matter Is Not Independent or Distinct

It is respectfully submitted that the restriction requirement as among Groups I-XXIV (hereinafter Group 1), among Groups XXV-XXXII (hereinafter Group 2) and among groups XXXIII-XL (hereinafter Group 3) is improper. It is respectfully submitted that the Restriction Requirement should be redrawn and set forth in three groups as follows:

Group 1, claims 1-24 and 36 directed to a method of treating neovascular disease of the eye by administering a targeted photosensitizing agent that binds to abnormal endothelium, and illuminating the tissue to cause damage thereto;

Group 2, claims 25-27 directed to a method of treating neovascular disease of the eye by administering a first targeted photosensitizing compound that selectively binds to a first targeted tissue, and administering a second targeted photosensitizing compound that selectively binds to a second targeted tissue; and, and illuminating both tissues to cause damage thereto; and

Group 3, claims 28-35 and 37 directed to kits and method of instructing in the use of the kit.

If deemed appropriate, an election of species in each elected group could be required for search purposes. It is noted, however, that election of species with respect to the photosensitizer is not correct. Election of species may only be required when more than one independent and distinct species are claimed or where at least one independent and distinct species is claimed together with a genus. The application presently provides generic claims as it relates to a photosensitizer. The Office can not impute a limitation to the claims from the disclosure.

Arguments

The test for the propriety of a restriction requirement is two-pronged. The first is whether the claimed subject matter is independent or distinct; and the second, is whether there is burden on the Office to examine all claims in the same application.

First, notwithstanding the arguments below, claim 13 belongs in the group XVI as set forth by the Office. Claim 13 recites:

> The method of claim 11, wherein the ligand is selected from the group consisting of: the ED-B domain of fibronectin; antibody specifically elicited to ED-B domain of fibronectin; VEGF; VEGF receptor; and $\alpha v\beta 3$ integrin

. . . second component of the bindable pair is selected from the group consisting of: receptor present on abnormal endothelium; ligand bindable to receptor present on abnormal endothelium; antigen present on abnormal endothelium; and antibody bindable to antigen present on abnormal endothelium.

The VEGF receptor, which is part of the elected species, is a receptor present on the abnormal endothelium. Thus, claim 13 belongs in group XVI.

With respect to the Restriction Requirement, it is alleged that the claimed subject matter of Groups I-XXXII are unrelated because they are directed to different methods of treating different diseases that differ with respect to their etiology, using distinct products that differ with respect to their structures and target specificity. The Examiner further alleges that the claimed subject matter of Groups XXXIII-XL are unrelated because the Examiner asserts that the products claimed differ with respect to their structure, target specificity, and biophysiochemistry and are therefore patently distinct. It is respectfully submitted that, with respect to all groups, the premise upon which the requirement is based is incorrect.

All of Groups I-XXIV and Groups XXV-XXXII are directed methods of treatment of neovascular diseases of the eye using a targeted photosensitizing agent. The last set of claims, Groups XXXIII-XL are directed to kits. Such methods and kits, while possibly containing distinct species (and as noted above, two different methods), are not directed to separate and distinct subject matter.

As discussed below, the diseases share an underlying pathology (abnormal neovasculature) and all of the targeted photosensitizing agents are selected to target the same cells (cells of the endothelium that line the neovasculature). For purposes of the following discussion reference is made to the "group 1," which encompasses the elected subject matter, as outlined above.

Group 1

Claim 1 is directed to a method for treating neovascular disease of the eye

the neosvaculature tissue with light for a period of time sufficient to activate the photosensitizing compound thereby causing damage to neovasculature tissue. Dependent claims specify the particular disease that involves neovascularization (claims 5-10), the type of illumination (claims 2 and 3), targeting agent that targets the photosensitizing agent to endothelium that lines the neovasculature tissue.

Neovascularization or proliferative angiogenesis is the process by which new blood vessels form. Except for processes, such as reproduction and during embryonic development, neovascularization is generally associated with abnormal conditions. It is known to those of skill in this art that numerous ocular diseases involve ocular neovascularization. These include age related macular degeneration (ARMD), proliferative diabetic retinopathies, neovascularization associated with tumors (see, *e.g.*, U.S. Patent Nos. 6,147,060, 6,127,401, 6,100,282, 6,090,944, 6,066,648 among many others). Hence the diseases, while different, are manifestations of the same pathology, neovascularization, that is targeted by the claimed method.

It is also known to those of skill in the art that neovasculature expresses receptors and antigens, such as α_v integrins and VEGF receptors (see, *e.g.*, the above listed patents). Sustained growth and metastasis of a variety of tumors has been shown to be dependent on the growth of new host blood vessels into the tumor in response to tumor derived angiogenic factors. Proliferation of new blood vessels in response to a variety of stimuli occurs as the dominant finding in the majority of eye diseases that blind, such as, but are not limited to, proliferative diabetic retinopathy (PDR), ARMD, rubeotic glaucoma, interstitial keratitis and retinopathy of prematurity. In these diseases, tissue damage can stimulate release of angiogenic factors resulting in capillary proliferation. Hence abnormal neovasculature is associated with a variety of ocular abnormalities and diseases that share a common underlying pathology and in such tissues a number of [illegible] integrins are upregulated. The instant methods

Thus, the claims are not directed to different methods of treating different diseases that differ with respect to their etiology, using distinct products that differ with respect to their structures and target specificity. The methods are for treating a common underlying pathology using products that target the same tissue. The instant claims are directed to methods that treat ocular conditions that involve neovascularization by destroying the neovasculature by targeting photosensitizing agents to the endothelium lining of such neovasculature, and destroying it. The targeting is effected using agents that cause the photosensitizing compounds to be delivered to the endothelium, and employ ligands that specifically bind to receptors that are expressed thereon.

Therefore, the claims are directed, not to the treatment of a diverse diseases using diverse agents that do not share common structural features, but are directed to the methods for destroying ocular neovasculature by targeting photosensitizing agents to the neovasculature. The dependent claims, thus, are not directed to distinct "inventions," but are directed to embodiments of the same invention.

What the Examiner has characterized as different restrictable groups are dependent claims directed to specific embodiments of the claimed subject matter. The dependent claims specify ways of activating the photosensitizer, types of targeting strategies, and different diseases that share this common underlying pathology. This subject matter does not warrant multiple patents, and certainly not thirty-seven patents.

In addition, by setting up the requirement as a restriction requirement rather than an election of species, there is no group that encompasses the generic method as set forth in claims 1, 25 and 28. Not only is it not reasonable to require the applicant to obtain 37 patents to cover some of the subject matter claimed in the application, it is unfair to deny coverage to all of it, by setting up a restriction requirement that eliminates the possibility of generic coverage. Therefore, the [illegible] forth is incomplete since all claim subject matter is

Furthermore, with the requirement as set forth, applicant could ultimately obtain a multitude of patents, each to one of the groups, that expire on different days. Since the Office has determined that claims to different photosensitizing compounds, claims to different neovascular diseases of the eye, and claims to different targeting mechanisms such as antibodies, antigens, and receptors, are separate species, multiple patents could issue. Obviousness-type double patenting could not be asserted in this situation, and a later-issuing patent could possibly extend patent coverage. See MPEP 806, paragraph 3, which states:

> [w]here inventions are related as disclosed but are not distinct as claimed, restriction is never proper. Since, if restriction is required by the Office double patenting cannot be held, it is imperative the requirement should never be made where related inventions as claimed are not distinct.

See, also MPEP 804.01, which states:

> 35 U.S.C.121, third sentence, provides that wherein the Office requires restriction, the patent of either the parent or any divisional application thereof conforming to the requirement cannot be used as a reference against the other. This apparent nullification of double patenting as ground of rejection or invalidity in such cases imposes a heavy burden on the Office to guard against erroneous requirements for restriction where the claims define essentially the same inventions in different language and which, if acquiesced in, might result in the issuance of several patents for the same invention.

Thus obviousness-type double patenting cannot between a claim that recites:

> A method to treat neovascular disease of the eye, comprising:
> administering a targeted photosensitizing compound that selectively binds to abnormal endothelium that lines or composes neovasculature tissue; and
> illuminating the neosvaculature tissue with light for a period of time sufficient to activate the photosensitizing compound thereby causing damage to neovasculature tissue, wherein the photosensitizer is chlorin linked to antibody to VEGF receptor, and the disease is diabetic retinopathy.

A method to treat neovascular disease of the eye, comprising:
administering a targeted photosensitizing compound that selectively binds to abnormal endothelium that lines or composes neovasculature tissue; and
illuminating the neosvaculature tissue with light for a period of

linked to antibody to VEGF receptor, and the disease is macular degeneration.

In such methods, the same agent is targeted to neovasculature. The difference is the choice of subject to be treated. In one the disease involving neovascularization is diabetic retinopathy, in the other the disease is macular degeneration.

No Burden on the Office

As discussed above, the subject matter as divided by the Office is not independent or distinct. In addition, it is respectfully submitted that the Office has failed to demonstrate that there is a serious burden necessitating such extensive restriction (see MPEP 803.02; 806.04(a)).

Applicant is entitled to have more than one claim per application examined; in this instance there are 37 claims and a 37-way restriction requirement. It cannot be a burden to examine the claims grouped as suggested above if an election of species is imposed. The application includes 37 claims drafted in traditional manner of differing scope. Applicant is entitled to claim the subject matter under one or more claims of varying scope. Under U.S. patent practice, an applicant is not required to claim each and every embodiment of the subject matter they wish to protect as separate single claimed embodiments and in different patents. Thus, this restriction is improper.

Also, the fact that subject matter has different primary classifications is evidentiary of a burden, but not conclusive and is not demonstrative of a serious burden. The mandatory search for each of the groups is, if not identical, substantially coincident. For example, the Office has indicated that Groups I through XXIV have been identified as having claimed subject matter classified in Class 424, subclasses 193.1 and 9.51; that Groups XXV through XXXII have been identified as having claimed subject matter classified in Class 424, subclasses 9.51 and 9.34; and Groups XXXIII through XL have been identified as having claimed subject matter classified in Class 435, subclass 810 and Class 424, subclasses

XXXII; or XXXIII through XL. In fact, the Examiner would be required to search Class 424, subclass 9.51 for all indicated Groups (I through XL). The Examiner has further indicated that a search would be required in the same subclasses 193.1 and 9.51 of Class 424 for all of Groups 1 through XXIV and XXXIII through XL. Thus, there is no burden on the Office to search and examine the claimed subject matter.

* * *

In view of the remarks herein, withdrawal of the requirement for restriction as drafted, and examination of the application on the merits are respectfully requested.

Respectfully submitted,
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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MARKED-UP CLAIMS (37 C.F.R. § 1.121)

Please amend claim 1 as follows:

1. (Amended) A method to treat neovascular disease of the eye, comprising:

administering a targeted photosensitizing compound [which] that selectively binds to abnormal endothelium that lines or composes neovasculature tissue; and

illuminating the neosvaculature tissue with light for a period of time sufficient to activate the photosensitizing compound thereby causing damage to neovasculature tissue, but without impairing or destroying other tissue.